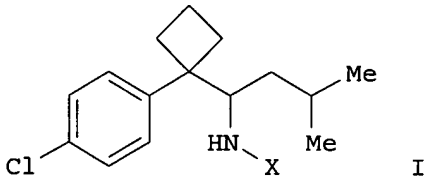
EXAMINER'S SEARCH NOTES

L3 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:526047 CAPLUS
DN 135:122299
TI Synthesis of racemic and optically pure desmethylsibutramine, didesmethylsibutramine, oral formulations comprised thereof and their use as dopamine reuptake inhibitors
IN Senanayake, Chrisantha H.; Fang, Qun K.; Han, Zhengxu; Krishnamurthy, Dhileepkumar
PA Sepracor Inc., USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001051453	A1	20010719	WO 2001-US762	20010110
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6399826	B1	20020604	US 2000-480889	20000111
	CA 2396950	AA	20010719	CA 2001-2396950	20010110
	EP 1246789	A1	20021009	EP 2001-901941	20010110
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003519675	T2	20030624	JP 2001-551835	20010110
PRAI	US 2000-480889	A	20000111		
	US 1999-372158	A2	19990811	bad date	
	WO 2001-US762	W	20010110		

OS MARPAT 135:122299
GI



I

AB Racemic and optically pure **sibutramine** metabolites, desmethyl- (I, X = Me) and didesmethylsibutramine I (X = H; II) were prepared Addition of i-butylmagnesium bromide to 1-(4-chlorophenyl)cyclobutanecarbonitrile followed by MeOH quench and treatment with NaBH4 produced II. II was converted to the N-formyl derivative and reduced to give I. Resolution with (R)-mandelic acid furnished (R)-I. **Sibutramine** isomers are inhibitors of norepinephrine (NE) and 5-HT uptake and bind to muscarinic receptors while metabolites I and II were found to have affinity for NE, 5-HT and negligible activity at muscarinic sites. At NE reuptake sites, (+)-I had IC50 = 4 nM (vs. (-)-I IC50 = 870 nM), and reuptake site binding selectivity for NE/5-HT = 12. A lactose free solid oral dosage hard gelatin capsule and tablet formulation was provided. Methods to treat **neuropathic pain** and diabetic peripheral neuropathy were claimed.

L3 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:51989 CAPLUS
DN 136:96083
TI Methods of using and compositions comprising (+)-**sibutramine** optionally in combination with other pharmacologically active compounds
IN Young, James W.; Jerussi, Thomas P.
PA USA
SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U. S. Ser. No. 442,263.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002006964	A1	20020117	US 2001-770393	20010129
	WO 2002060427	A2	20020808	WO 2002-US2038	20020123
	WO 2002060427	A3	20030213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2003078303	A1	20030424	US 2002-295871	20021118
PRAI	US 1995-442263	A2	19950516		
	US 2001-770393	A	20010129		

AB This invention encompasses methods for the treatment and prevention of disorders that include, but are not limited to, eating disorders; weight gain; obesity; irritable bowel syndrome; obsessive-compulsive disorders; platelet adhesion; apnea; affective disorders such as attention deficit disorders, depression, and anxiety; male and female sexual function disorders; restless leg syndrome; osteoarthritis; substance abuse including nicotine and cocaine addiction; narcolepsy; pain such as **neuropathic pain**, diabetic neuropathy, and chronic pain; migraines; cerebral function disorders; chronic disorders such as premenstrual syndrome; and incontinence. The invention further encompasses pharmaceutical compns. and dosage forms which comprise optically pure (+)-**sibutramine**, optionally in combination with a phosphodiesterase inhibitor or a lipase inhibitor.

L3 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:51988 CAPLUS
DN 136:107551
TI Method of using and compositions comprising (-) **sibutramine** optionally in combination with other pharmacologically active compounds
IN Young, James W.; Jerussi, Thomas P.
PA USA
SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 721,669.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002006963	A1	20020117	US 2001-770665	20010129
WO 2002060428	A2	20020808	WO 2002-US2039	20020123
WO 2002060428	A3	20021219		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 1992-903040 ahn B1 19920623
US 1995-461608 ahn B1 19950605
US 2000-721669 ahn A2 20001127
US 2001-770665 ahn A 20010129

AB This invention encompasses methods for the treatment and prevention of disorders that include, but are not limited to, eating disorders; weight gain; obesity; irritable bowel syndrome; obsessive-compulsive disorders; platelet adhesion; apnea; affective disorders such as attention deficit disorders, depression, and anxiety; male and female sexual function disorders; restless leg syndrome; osteoarthritis; substance abuse including nicotine and cocaine addiction; narcolepsy; pain such as **neuropathic pain**, diabetic neuropathy, and chronic pain; migraines; cerebral function disorders; chronic disorders such as premenstrual syndrome; and incontinence. The invention further encompasses pharmaceutical compns. and dosage forms which comprise optically pure (-) **sibutramine**, optionally in combination with a phosphodiesterase inhibitor or a lipase inhibitor. A solution of 21.7 g L-dibenzyltartaric acid ("L-DBTA") in Et acetate was added to a solution of 12.3 g racemic **sibutramine** in Et acetate and the reaction mixture was heated to reflux and cooled to room temperature The white precipitate was collected and the solid was then suspended in Et acetate and heated at reflux for 30 min. The solid was collected and further crystallized in iso-Pr alc. to give 11.3 g of (-)-**sibutramine** L-DBTA (yield 76%). Free base was obtained by treatment of (-)-**sibutramine** L-DBTA with saturated aqueous NaHCO3 and extracted with chloroform. A pharmacol. study was conducted to determine the relative potency, comparative efficacy, binding affinity, and toxicity of the enantiomers and racemic mixture of **sibutramine**. A capsule contained (-) **sibutramine** 10.0, lactose 70.0, corn starch 19.5, and magnesium stearate 0.05 mg.